Remarks

Claims 41-51 are pending in this application. No claim amendments are made in this paper, and thus, no new matter has been introduced. Applicant respectfully submits that all of the pending claims are allowable for at least the following reasons.

A. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

In the Office Action, the rejection of claims 41-51 as being unpatentable over Scott *et al.*, *Br. J. Pharmacol.*, 111: 97-102 (1994) ("Scott"), in view of WO 94/00114 by Young *et al.* ("Young") and Adda *et al.*, *Arq. Neuropsiquiatr.* 55(3A): 423-6 (1997) (abstract only) ("Adda") is maintained. Applicant respectfully traverses this rejection.

The current standard of obviousness takes into account (1) whether there would have been a "reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does;" and (2) whether there would have been a reasonable expectation of success. (*See e.g., PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007) ("The burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed process, and would have had a reasonable expectation of success in doing so.") (internal quotations omitted)).

At the outset, Applicant respectfully reiterates that the claims are not obvious for at least the reasons set forth in the previous response of November 12, 2008, which is incorporated herein by reference. Specifically, Applicant respectfully submits that (1) none of the cited references discloses or suggests the use of enantiomerically pure (S)-didesmethylsibutramine; and (2) none of the references cited in the Office Action discloses anything about the use of an anti-depressant, much less enantiomerically pure (S)-didesmethylsibutramine, for the treatment of narcolepsy.

In response, it is asserted in the Office Action that Applicant's submission is unpersuasive, allegedly because "KSR state[s] that '**obvious to try**' can be a motivation . . . where an artisan is faced with a choice of choosing from . . . racemate didesmethylsibutramine [or its pure enatiomers], which are directed to achieving predictable

solutions . . . with a reasonable expectation of success."[1] (Office Action, page 8, emphasis in original).

In this regard, Applicant respectfully submits that while Scott discloses racemic didesmethylsibutramine, it does not disclose (S) isomer of didesmethylsibutramine. This submission is recognized and acknowledged in the current rejection, and was relied upon at least in part as the basis for the previously withdrawn rejection. (Office Action, page 5; Office Action dated September 24, 2008, pages 2-3). Further, the Examiner appears to assume that arriving at the claimed methods solely rests upon the determination that optically pure (S)-didesmethylsibutramine may be useful. However, this assumption wholly ignores the fact that there are numerous other disorders than narcolepsy[2] known in connection with racemic didesmethylsibutramine. In other words, to arrive at the methods recited by the pending claims, one would have had to: 1) arrive at the specific isomer recited by the claims; and 2) arrive at narcolepsy among numerous disorders. Thus, contrary to what the Examiner appears to believes, "obvious to try" cannot be the basis for obviousness in this case because one skilled in the art was not faced with "a finite number of identified, predictable solutions, with a reasonable expectation of success." (*See KSR International Co. v. Teleflex Inc.* 127 S.Ct. 1727, 1727 (2007) (providing that obvious to try rationale only appropriate where "one skilled in the art is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success")).

Moreover, Applicant respectfully submits that there is no basis provided in the Office Action to support the allegation that "racemate didesmethylsibutramine [or its pure enatiomers] . . . are directed to achieving predictable solutions . . . with a reasonable expectation of success." As presented in Applicant's previous response of May 30, 2008, which is incorporated herein by reference, case law is clear that any allegation asserting that a claimed enantiomer, or its method of use, is obvious in light of its racemate must first establish, on its particularized facts, that a person of ordinary skill would have had a reasonable expectation of success in both isolating the claimed enantiomer and using the compound for the purpose recited by the claims. (*See Forest Labs., Inc. v. Ivax*

---

[1] Further in this regard, Applicant respectfully submits that while the Office Action conclusively states that there was a reasonable expectation of success, no reasoning or basis is provided in this connection. Thus, the Office Action fails to address the well-established legal principle that "there is no basis to 'predict with a reasonable expectation of success whether one enantiomer of [the claimed compound] would have better pharmaceutical properties than the racemate itself.' (*see Sanofi-Synthelabo v. Apotex, Inc.*, 492 F.Supp.2d 353, 390 (S.D.N.Y 2007))"

[2] Indeed, as discussed below, there was no teaching or suggestion in prior art that would have even associated narcolepsy with racemic didesmethylsibutramine.

Pharmaceuticals, Inc., 438 F.Supp.2d 479, 493 (D. Del. 2006) (providing "unpredictable nature of the separation of racemic compounds" meant that "a person skilled in the art seeking such a resolution would not have a reasonable expectation of success without undue experimentation.") (emphasis added)) (*see also Sanofi-Synthelabo v. Apotex, Inc.*, 492 F.Supp.2d 353, 390 (S.D.N.Y 2007) (providing that "the prior art did not enable a person of ordinary skill in the art to predict with a reasonable expectation of success whether one enantiomer of [the claimed compound] would have better pharmaceutical properties than the racemate itself . . . .") (emphasis added)) (*see also Ex parte Young* (B.P.A.I. Appeal No. 2004-1592) (holding that the enantiomer claims to be nonobvious and patentable in light of previously disclosed in its racemic form)).

In fact, in "Response to applicant's arguments/remarks" section of the Office Action dated September 24, 2008, the Examiner acknowledged the following submissions made by Applicant:

> The cited references fail to establish that there would have been a reasonable expectation that (S)-didesmethylsibutramine would have "better" pharmaceutical properties than racemic didesmethylsibutramine or racemic sibutramine.
>
> . . . .
>
> . . . [T]he Court [in *Ex parte Young*] found that no reasonable expectation of success in arriving at appellants claimed method of treatment using a single enantiomer of a pharmaceutical which was previously discloses in racemic form.
>
> . . . .
>
> A person skilled in the art would have no basis to "predict with a reasonable expectation of success whether one enantiomer of the claimed compound would have better pharmaceutical properties than the racemate itself.["]

Based in part on these submissions, the Examiner withdrew the rejection. (Office Action dated September 24, 2008, pages 2-3) ("In response, the rejection is withdrawn." (emphasis added)). Thus, the allegation in the current Office Action that "racemate didesmethylsibutramine [or its pure enatiomers] . . . are directed to achieving predictable solutions with a reasonable expectation of success" is not only incorrect, but also seemingly inconsistent with the withdrawal of the rejection in the previous Office Action dated September 24, 2008.

Further, it is asserted in the Office Action that Applicant's previous response is unpersuasive, allegedly because "Adda . . . teach[es] that there is a nexus between narcolepsy and depressive symptoms" and that "patients with narcolepsy are susceptible to depression as evidence by the teaching of Adda." (Office Action, pages 9-10). It is further alleged that "the instant claimed narcolepsy population does not preclude a narcolepsy patient from also developing depressive symptoms." (*Id.*, pages 9-10).

In this regard, Applicant respectfully reiterates that Adda clearly discloses that depression is not a major symptom commonly associated with all narcolepsy patients. Specifically, Adda discloses that 75% of the studied cases showed no depressive disorder and concluded that there is "no correlation between narcolepsy and major depression." (*See* Adda). Contrary to what is alleged in the Office Action, there is no disclosure in Adda providing a nexus between narcolepsy and depressive symptoms. Nor does Adda disclose or suggest that patients with narcolepsy are susceptible to depression. Quite to the contrary, Adda actually teaches that there is no correlation between depression and narcolepsy. In fact, as Applicant has pointed out previously, none of the references cited in the Office Action discloses anything about the use of an anti-depressant, much less optically pure (S)-didesmethylsibutramine, for the treatment of narcolepsy. The allegation that the instant claimed narcolepsy population does not preclude a narcolepsy patient from also developing depressive symptoms is equivalent to stating that, for example, a cancer patient is not precluded from also developing depression. By this logic, an antidepressant should be an effective treatment for cancer, which is clearly nonsensical. Therefore, Applicant respectfully submits that the allegations set forth in the Office Action do not provide a reasonable basis for a skilled artisan to use an anti-depressant, much less enantiomerically pure (S)-didesmethylsibutramine, for the treatment of narcolepsy.

Further, it is asserted in the Office Action that Applicant's previous response is unpersuasive, allegedly because "the facts of the instant case are distinguishable from the facts in *Rapoport v. Dement*[,]" 254 F.3d 1053 (Fed. Cir. 2001) (Office Action, pages 10-11). It is further alleged that "the symptom of depression is not severable from narcolepsy but is related to the underlined narcoleptic condition such that one would reasonably expect to successfully control the symptoms associated with narcolepsy with optically pure (S)-didesmethylsibutramine absent objective evidence to the contrary."

In this regard, Applicant respectfully submits that the Examiner's allegation that "the symptom of depression is not severable from narcolepsy" has no basis, especially in view of the fact that Adda clearly discloses that there is no correlation between narcolepsy

and depression. In other words, Adda clearly discloses that any depression that narcolepsy patients encounter is a non-major symptom of narcolepsy. Thus, there certainly could not have been any expectation that narcolepsy could be treated by treating a non-major symptom of narcolepsy, *i.e.*, depression. Accordingly, Applicant submits that the holdings set forth in *Rapoport* are entirely applicable to the current application.

Further in this regard, Applicant respectfully reiterates that case law is clear that the patentability of claims to the treatment of a disorder is not negated by prior disclosure of the treatment of the symptoms associated with the disorder. (*See, e.g.*, *Rapoport* 254 F.3d. at 1060-1061 (holding the reference's mention of the possibility of administering the compound to patients suffering from sleep apnea was "for the purpose of treating [a symptom] in such patients, not for the purpose of treating the sleep apnea disorder itself.")). Thus, use of an anti-depressant to treat depression as a symptom of narcolepsy would not have rendered obvious the use of an anti-depressant, much less enantiomerically pure (S)-didesmethylsibutramine, for the treatment of narcolepsy. That is because any administration of an anti-depressant would have been "for the purpose of treating [depression]," but not for the purpose of treating narcolepsy. (*Id.*). For this additional reason, Applicant respectfully submits that the rejection of the claims should be withdrawn.

B. Conclusion

For at least the foregoing reasons, Applicant submits that all of the pending claims are allowable, and thus, respectfully requests that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

No fee is believed due for this submission except for a fee of $540 due for filing the Notice of Appeal. If any other fees are require for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

Date May 4, 2009

Hoon Choi (Reg. No. 64,214)
For: Anthony M. Insogna (Reg. No. 35,203)
Jones Day
12265 El Camino Real, Suite 200
San Diego, CA 92130
(858) 314-1200